Applicants provide with this response evidence of Budapest Treaty deposits of the requisite hybridomas with the International Deposit Authority (Appendices A.1 and A.2). Upon issuance of the present application, all restrictions upon availability of the deposited hybridomas are irrevocably removed, although Applicants retain the right to be notified of the identity of requestors of the deposited hybridomas.

In view of the revision of claim 20 and the submission of this evidence, Applicants submit that a skilled artisan, informed by the present specification, would be able to practice the present invention without undue experimentation. Accordingly, Applicants respectfully request reconsideration and withdrawal of the above rejections.

Rejections Under 35 U.S.C. § 102

In alleging lack of novelty, the Examiner rejected claims 13-14 and 20-22 as being anticipated by Mawby *et al. (Biochem. J.* **304**:525-530, 1994; Mawby). In addition, the Examiner also rejected these claims as being anticipated by Lindberg *et al.* (*J. Cell Biol.* **123**:485-196, 1993), as evidenced by Petterson *et al.* (*Apoptosis* **5**:299-306, 2000; Pettersen 2000). Applicants respectfully traverse these rejections.

Mawby teaches a BRIC-125 mAb, an anti-CD47mAb similar to the anti-Integrin Associated Protein (IAP) antibody and ovarian tumor marker (OA3) antibody. Mawby, however, does not teach an IAP antibody that is capable of inducing apoptosis in nucleated blood cells.

In the present Office Action, the Examiner alleges that it would be inherent that Mawby's antibody would induce apoptosis. Contrary to this assertion, Pettersen *et al.* (*J. Immunol.* **162**:7031-40, 1999) and Pettersen (2000) showed that not all anti-CD47 antibodies possess an anti-apoptotic property. As exemplified in Pettersen (1999), a copy of which is enclosed with this response (Appendix B), and Pettersen (2000), CD47 antibodies, such as 2D3 and B6H12, fail to induce apoptosis. Moreover, Pettersen (1999) reasoned that a "distinct conformation or conformational change [in the anti-CD47 antibody] is required for death signaling" to occur. A person of ordinary skill in the art, upon reading Mawby, would not be informed that an anti-CD47 antibody can cause apoptosis of nucleated blood cells. Since Mawby fails to

disclose an antibody with anti-apoptotic activity, it is not a proper patent-defeating reference to the claimed invention.

The Examiner further alleges that Lindberg teaches "a monoclonal antibody, 1F7, that binds to human IAP and, as evidenced by Pettersen (2000), 1F7 causes apoptosis." Applicants respectfully disagree with the Examiner.

First of all, prior to the filing of the present application, the apoptotic property of an anti-IAP antibody was not known. Again, those skilled in the art failed to recognize the inherent property of these anti-IAP antibodies. Moreover, based on Pettersen's own disclosure, not all of the anti-CD47 anibodies are capable of causing the death of nucleated blood cells. Moreover, Applicants have amended claim 13 to exclude Pettersen's 1F7 antibody. Amended claim 13 does not read on 1F7. Accordingly, Lindberg does not anticipate the claimed invention.

In light of the above remarks and claim amendments, the Examiner has not established a prima facie case of anticipation that Mawby and Lindberg, along with Pettersen (2000), disclose each and every element of the claimed invention. They are, therefore, not patent-defeating references . Hence, reconsideration and withdrawal of the rejections under Section 102 are earnestly requested.

Rejection Under 35 U.S.C. § 103

The Examiner rejected claim 13-18 and 20-23 as being unpatentable over Lindberg *et al.*, as evidenced by Pettersen *et al.* (2000), as applied to claims 3-14 and 20-22 above, and further in view of Goding (*Monoclonal Antibodies: Principles and Practice, Second Ed.*, pages 125-129, 1986).

According to the Examiner, Lindberg "does not specifically teach a hybridoma or fragments of the [claimed] antibody" and that "this deficiency" is made up by Goding's teachings. The rejection is respectfully traversed.

The Examiner has failed to establish a *prima facie* case of obviousness with respect to the claimed invention. The rejection must show all of the recited claim elements in the combination of references that underscore the rejection. When combining elements to make out a *prima facie* case of obviousness, that is, the Examiner is obliged to show by reference to specific evidence in the cited references

that there was (i) a suggestion to make the combination and (ii) a reasonable expectation that the combination would succeed. Both suggestion and reasonable expectation must be found within the prior art, and not be gleaned from Applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed Cir. 1988).

As stated in the earlier sections, both Lindberg *et al* and Pettersen *et al.* (2000) are not anticipatory to the claimed invention.

Applicants submit that it would not have been obvious to one of ordinary skill in the art at the time the claimed invention was made to produce antigen-binding fragments of Linderg's antibody, via the method of Goding. Neither is there any suggestion nor motivation to modify the teachings of the Lindberg with Goding's methods to produce the antigenic fragments of the claimed anti-IAP antibody. Thus, the Examiner has failed to support his alleged case of *prima facie* obviousness, and as a result of these deficiencies, it is respectfully requested that this rejection be withdrawn.

CONCLUSION

In view of the foregoing, it is respectfully urged that the present claims are in condition for allowance. An early notice to this effect is earnestly solicited. Should there be any questions regarding this application, the Examiner is invited to contact the undersigned at the telephone number shown below.

Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.

Respectfully submitted,

Date: May 7, 2002

By _____

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

13. (Amended) A monoclonal antibody [capable of inducing apoptosis of nucleated blood cells with Integrin Associated Protein (IAP) through binding to IAP] that specifically recognizes and binds to an Integrin Associated Protein, wherein the binding of said monoclonal antibody to said Integrin Associated Protein induces apoptosis of nucleated blood cells and wherein said monoclonal antibody is other than 1F7.

18. (Amended) A hybridoma that produces a monoclonal antibody as defined in claim [15] 14.

20. (Amended) An antileukemic agent, comprising [a substance that binds to IAP and stimulates the action of IAP to induce] a monoclonal antibody or a fragment thereof that specifically recognizes and binds to an Integrin Associated Protein, wherein said binding of said monoclonal antibody or said fragment thereof induces [the] apoptosis of nucleated blood cells.